(c) a selectable marker located between the first polynucleotide sequence and the second polynucleotide sequence,

wherein the targeting construct when introduced into murine embryonic stem cells, results in a transgenic mouse having a disruption in a retina-specific nuclear receptor gene, wherein the mouse when homozygous for a disruption in a retina-specific nuclear receptor gene exhibits an eye abnormality.

39. (New) The targeting construct of claim 38, wherein the targeting construct further comprises a screening marker, the screening marker positioned outside either the first polynucleotide sequence or the second polynucleotide sequence and opposite the selectable marker.

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40. (New) A method of producing a targeting construct for a retina-specific nuclear receptor gene, the method comprising:

(a) obtaining a first polynucleotide sequence homologous to a first region of a target gene;

(b) obtaining a second polynucleotide sequence homologous to a second region of the target gene;

(c) providing a vector comprising selectable marker; and

(d) inserting the first and second sequences into the vector such that the selectable marker is located between the first and the second sequences to produce the targeting construct,

wherein the targeting construct when introduced into murine embryonic stem cells, results in a transgenic mouse having a disruption in a retina-specific nuclear receptor gene, wherein the mouse when homozygous for a disruption in a retina-specific nuclear receptor gene exhibits an eye abnormality.

41. (New) A method of producing a targeting construct for a retina-specific nuclear receptor gene, the method comprising:

(a) providing a polynucleotide sequence homologous to a target gene;

(b) generating two different fragments of the polynucleotide sequence;

(c) providing a vector having a gene encoding a selectable marker; and

(d) inserting the two different fragments into the vector such that the selectable marker is located between the two different fragments to produce the targeting construct, wherein the targeting construct when introduced into murine embryonic stem cells, results in a transgenic mouse having a disruption in a retina-specific nuclear receptor gene, wherein the mouse when homozygous for a disruption in a retina-specific nuclear receptor gene exhibits an eye abnormality.

42. (New) A method of producing a transgenic mouse comprising a homozygous disruption in a retina-specific nuclear receptor gene, the method comprising:

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(a) introducing a retina-specific nuclear receptor gene targeting construct into a cell;

(b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse comprising a homozygous disruption in a retina-specific nuclear receptor gene,

wherein the transgenic mouse exhibits an eye abnormality.

43. (New) A method of producing a transgenic mouse comprising a homozygous disruption in a retina-specific nuclear receptor gene, the method comprising:

(a) providing a mouse embryonic stem cell comprising a disrupted retina-specific nuclear receptor gene; and

(b) introducing the mouse embryonic stem cell into a pseudopregnant mouse, wherein the pseudopregnant mouse gives birth to a chimeric mouse; and

(c) breeding the chimeric mouse to produce the transgenic mouse,

wherein the transgenic mouse exhibits an eye abnormality.

44. (New) A transgenic mouse comprising a homozygous disruption in a retina-specific nuclear receptor gene, wherein the transgenic mouse exhibits an eye abnormality.

45. (New) The transgenic mouse of claim 44, wherein the eye abnormality is a retinal abnormality.

46. (New) The transgenic mouse of claim 45, wherein the retinal abnormality is characterized by retinal dysplasia.

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47. (New) The transgenic mouse of claim 46, wherein the transgenic mouse exhibits at least one of the following characteristics: rosette formation in the retina, retinal folding, segmental thinning or absence of the outer nuclear layer of the retina, or absence of the retina.

48. (New) A cell or tissue isolated from the transgenic mouse of claim 44.

49. (New) A transgenic mouse comprising a heterozygous disruption in a retina-specific nuclear receptor gene, wherein said disruption in a homozygous state inhibits production of a functional retina-specific nuclear receptor protein resulting in a transgenic mouse exhibiting an eye abnormality.

50. (New) A cell transformed with the targeting construct of claim 38, wherein the cell comprises a disruption in a retina-specific nuclear receptor gene.

REMARKS

I. Amendments

Claims 1-10 and 17-24 are canceled. New claims 38-50 are being added. The newly added claims do not add new matter and are completely supported by the application as originally filed. More particularly, support for claims 38-41 directed to a targeting construct and methods of producing the targeting construct can be found, for example, at page 12, lines 33-35, at page 18, lines 22-30 and page 59, lines 18-36 through page 60, line 9 of the specification. Additionally, support for claims 42-48 directed to transgenic mice exhibiting an eye abnormality and having a disruption in a retina-specific nuclear receptor gene, methods of producing said